Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19)

16-24 February 2020

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I. The Mission

Goal and Objectives

The overall goal of the Joint Mission was to rapidly inform national (China) and international planning on next steps in the response to the ongoing outbreak of the novel coronavirus disease (COVID-19[1]) and on next steps in readiness and preparedness for geographic areas not yet affected.

The major objectives of the Joint Mission were as follows:

- To enhance understanding of the evolving COVID-19 outbreak in China and the nature and impact of ongoing containment measures;
- To share knowledge on COVID-19 response and preparedness measures being implemented in countries affected by or at risk of importations of COVID-19;
- To generate recommendations for adjusting COVID-19 containment and response measures in China and internationally; and
- To establish priorities for a collaborative programme of work, research and development to address critical gaps in knowledge and response and readiness tools and activities.

Members & Method of Work

The Joint Mission consisted of 25 national and international experts from China, Germany, Japan, Korea, Nigeria, Russia, Singapore, the United States of America and the World Health Organization (WHO). The Joint Mission was headed by Dr Bruce Aylward of WHO and Dr Wannian Liang of the People's Republic of China. The full list of members and their affiliations is available in Annex A. The Joint Mission was implemented over a 9-day period from 16-24 February 2020. The schedule of work is available in Annex B.

The Joint Mission began with a detailed workshop with representatives of all of the principal ministries that are leading and/or contributing to the response in China through the National Prevention and Control Task Force. A series of in-depth meetings were then conducted with national level institutions responsible for the management, implementation and evaluation of the response, particularly the National Health Commission and the China Centers for Disease Control and Prevention (China CDC). To gain first-hand knowledge on the field level implementation and impact of the national and local response strategy, under a range of epidemiologic and provincial contexts, visits were conducted to Beijing Municipality and the provinces of Sichuan (Chengdu), Guangdong (Guangzhou, Shenzhen) and Hubei (Wuhan). The field visits included community centers and health clinics, country/district hospitals, COVID-19 designated hospitals, transportations hubs (air, rail, road), a wet market, pharmaceutical and personal protective equipment (PPE) stocks warehouses, research institutions, provincial health commissions, and local Centers for

[1] In the Chinese version of this report, COVID-19 is referred to throughout as novel coronavirus pneumonia or NCP, the term by which COVID-19 is most widely known in the People's Republic of China.

Disease Control (provincial and prefecture). During these visits, the team had detailed discussion and consultations with Provincial Governors, municipal Mayors, their emergency operations teams, senior scientists, frontline clinical, public health and community workers, and community neighbourhood administrators. The Joint Mission concluded with working sessions to consolidate findings, generate conclusions and propose suggested actions.

To achieve its goal, the Joint Mission gave particular focus to addressing key questions related to the natural history and severity of COVID-19, the transmission dynamics of the COVID-19 virus in different settings, and the impact of ongoing response measures in areas of high (community level), moderate (clusters) and low (sporadic cases or no cases) transmission.

The findings in this report are based on the Joint Mission's review of national and local governmental reports, discussions on control and prevention measures with national and local experts and response teams, and observations made and insights gained during site visits. The figures have been produced using information and data collected during site visits and with the agreement of the relevant groups. References are available for any information in this report that has already been published in journals.

The final report of the Joint Mission was submitted on 28 February 2020.

II. Major findings

The major findings are described in six sections: the virus, the outbreak, transmission dynamics, disease progression and severity, the China response and knowledge gaps. More detailed descriptions of technical findings are provided in Annex C.

The virus

On 30 December 2019, three bronchoalveolar lavage samples were collected from a patient with pneumonia of unknown etiology – a surveillance definition established following the SARS outbreak of 2002-2003 – in Wuhan Jinyintan Hospital. Real-time PCR (RT-PCR) assays on these samples were positive for pan-Betacoronavirus. Using Illumina and nanopore sequencing, the whole genome sequences of the virus were acquired. Bioinformatic analyses indicated that the virus had features typical of the coronavirus family and belonged to the Betacoronavirus 2B lineage. Alignment of the full-length genome sequence of the COVID-19 virus and other available genomes of Betacoronavirus showed the closest relationship was with the bat SARS-like coronavirus strain BatCov RaTG13, identity 96%.

Virus isolation was conducted with various cell lines, such as human airway epithelial cells, Vero E6, and Huh-7. Cytopathic effects (CPE) were observed 96 hours after inoculation. Typical crown-like particles were observed under transmission electron microscope (TEM) with negative staining. The cellular infectivity of the isolated viruses could be completely neutralized by the sera collected from convalescent patients. Transgenic human ACE2 mice and Rhesus monkey intranasally challenged by this virus isolate induced multifocal pneumonia with interstitial hyperplasia. The COVID-19 virus was subsequently detected and isolated in the lung and intestinal tissues of the challenged animals.

Whole genome sequencing analysis of 104 strains of the COVID-19 virus isolated from patients in different localities with symptom onset between the end of December 2019 and mid-February 2020 showed 99.9% homology, without significant mutation (Figure 1).

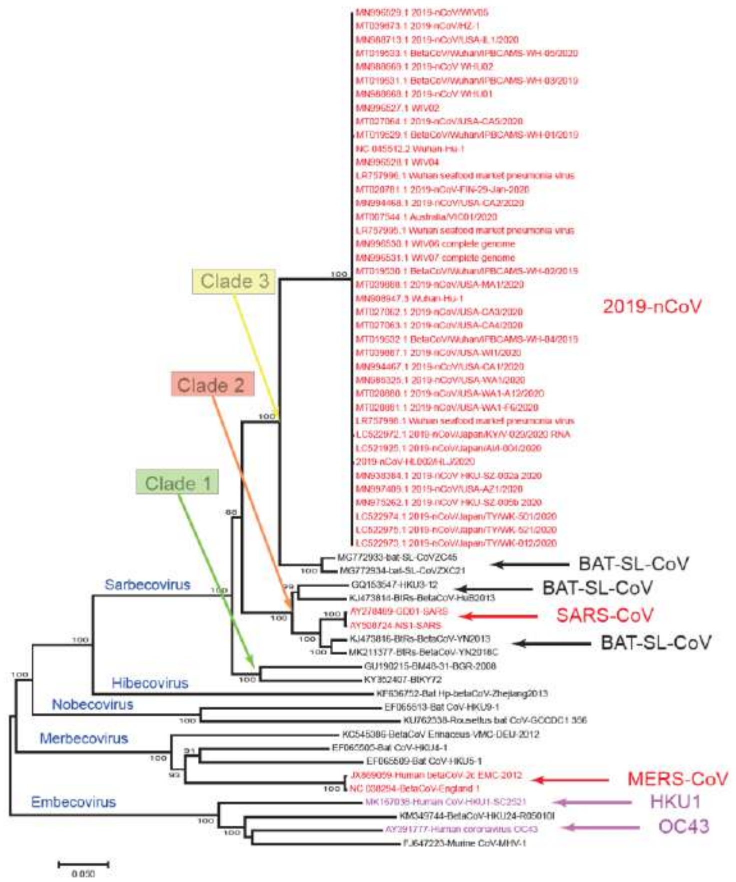


Figure 1. Phylogenetic analysis of the COVID-19 virus and its closely related reference genomes

Note: COVID-19 virus is referred to as 2019-nCoV in the figure, the interim virus name WHO announced early in the outbreak.

Post-mortem samples from a 50-year old male patient from Wuhan were taken from the lung, liver, and heart. Histological examination showed bilateral diffuse alveolar damage with cellular fibromyxoid exudates. The lung showed evident desquamation of pneumocytes and hyaline membrane formation, indicating acute respiratory distress syndrome (ARDS). Lung tissue also displayed cellular and fibromyxoid exudation, desquamation of pneumocytes and pulmonary oedema. Interstitial mononuclear inflammatory infiltrates, dominated by lymphocytes, were seen in both lungs. Multinucleated syncytial cells with atypical enlarged pneumocytes characterized by large nuclei, amphophilic granular cytoplasm, and prominent nucleoli were identified in the intra-alveolar spaces, showing viral cytopathic-like changes. No obvious intranuclear or intracytoplasmic viral inclusions were identified.

The outbreak

As of 20 February 2020, a cumulative total of 75,465 COVID-19 cases were reported in China. Reported cases are based on the National Reporting System (NRS) between the

National and Provincial Health Commissions. The NRS issues daily reports of newly recorded confirmed cases, deaths, suspected cases, and contacts. A daily report is provided by each province at 0300hr in which they report cases from the previous day.

The epidemic curves presented in Figures 2 and 3 are generated using China's National Infectious Disease Information System (IDIS), which requires each COVID-19 case to be reported electronically by the responsible doctor as soon as a case has been diagnosed. It includes cases that are reported as asymptomatic and data are updated in real time. Individual case reporting forms are downloaded after 2400hr daily. Epidemiologic curves for Wuhan, Hubei (outside of Wuhan), China (outside Hubei) and China by symptom onset are provided in Figure 2.

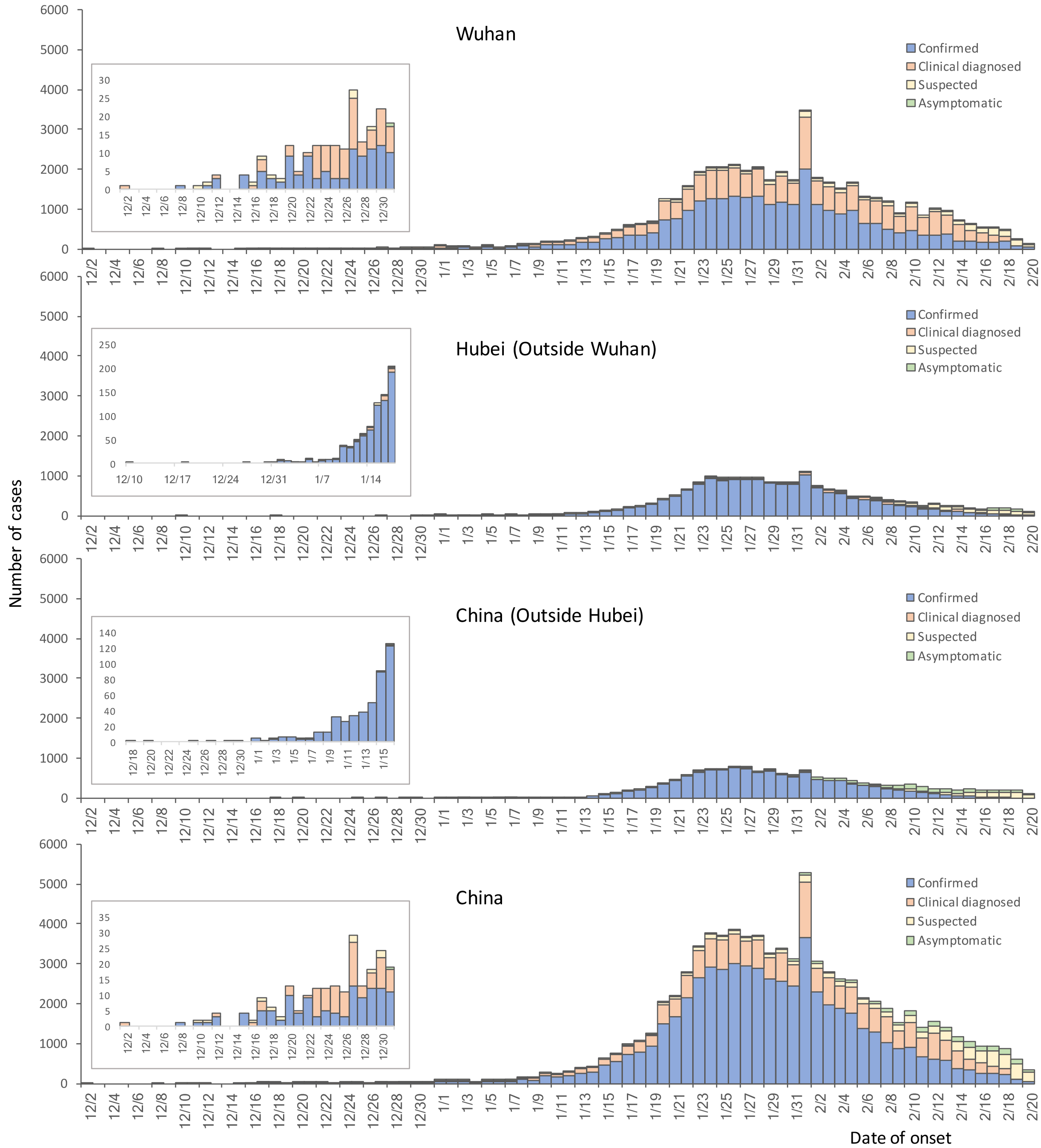


Figure 2 Epidemiologic curve of COVID-19 laboratory confirmed cases, by date of onset of illness, reported in China, as of 20 February 2020

Figure 3 presents epidemic curves of laboratory-confirmed cases, by symptom onset and separately by date of report, at 5, 12, and 20 February 2020. Figures 2 and 3 illustrate that the epidemic rapidly grew from 10-22 January, reported cases peaked and plateaued between 23 January and 27 January, and have been steadily declining since then, apart from the spike that was reported on 1 February (note: at a major hospital in Wuhan, fever clinic patients fell from a peak of 500/day in late January to average 50/day since mid-February).

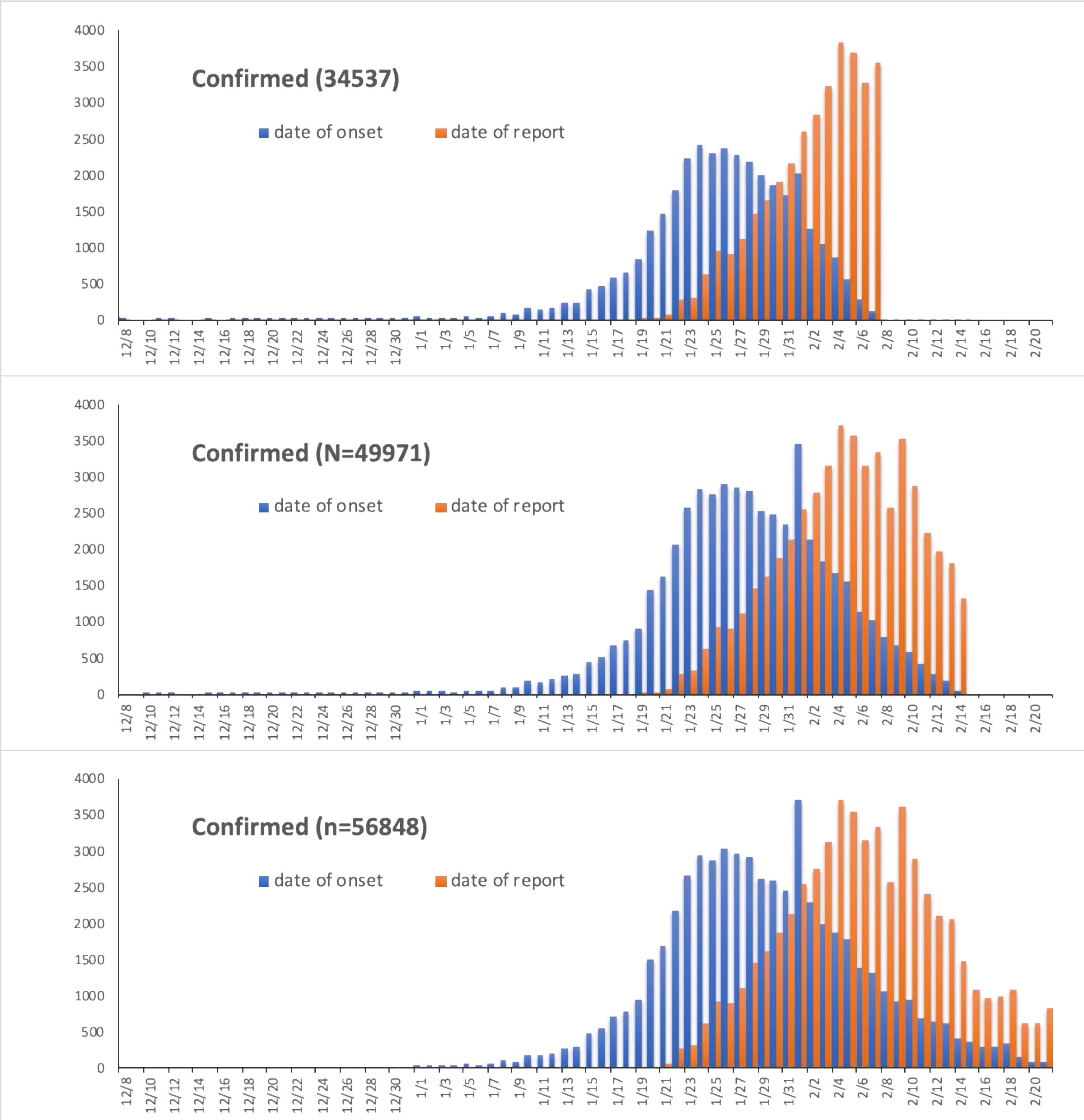


Figure 3. Epidemic curves by symptom onset and date of report as of 5 February (top panel), 12 February (middle panel) and 20 February 2020 (lower panel) for laboratory confirmed COVID-19 cases for all of China

Based on these epidemic curves, the published literature, and our on-site visits in Wuhan (Hubei), Guangdong (Shenzhen and Guangzhou), Sichuan (Chengdu), and Beijing, the Joint Mission team has made the following epidemiological observations:

Demographic characteristics

Among 55,924 laboratory confirmed cases reported as of 20 February 2020, the median age is 51 years (range 2 days-100 years old; IQR 39-63 years old) with the majority of cases (77.8%) aged between 30–69 years. Among reported cases, 51.1% are male, 77.0% are from Hubei and 21.6% are farmers or laborers by occupation.

Zoonotic origins

COVID-19 is a zoonotic virus. From phylogenetics analyses undertaken with available full genome sequences, bats appear to be the reservoir of COVID-19 virus, but the intermediate host(s) has not yet been identified. However, three important areas of work are already underway in China to inform our understanding of the zoonotic origin of this outbreak. These include early investigations of cases with symptom onset in Wuhan throughout December 2019, environmental sampling from the Huanan Wholesale Seafood Market and other area markets, and the collection of detailed records on the source and type of wildlife species sold at the Huanan market and the destination of those animals after the market was closed.

Routes of transmission

COVID-19 is transmitted via droplets and fomites during close unprotected contact between an infector and infectee. Airborne spread has not been reported for COVID-19 and it is not believed to be a major driver of transmission based on available evidence; however, it can be envisaged if certain aerosol-generating procedures are conducted in health care facilities. Fecal shedding has been demonstrated from some patients, and viable virus has been identified in a limited number of case reports. However, the fecal-oral route does not appear to be a driver of COVID-19 transmission; its role and significance for COVID-19 remains to be determined. Viral shedding is discussed in the Technical Findings (Annex C).

Household transmission

In China, human-to-human transmission of the COVID-19 virus is largely occurring in families. The Joint Mission received detailed information from the investigation of clusters and some household transmission studies, which are ongoing in a number of Provinces. Among 344 clusters involving 1308 cases (out of a total 1836 cases reported) in Guangdong Province and Sichuan Province, most clusters (78%-85%) have occurred in families. Household transmission studies are currently underway, but preliminary studies ongoing in Guangdong estimate the secondary attack rate in households ranges from 3-10%.

Contact Tracing

China has a policy of meticulous case and contact identification for COVID-19. For example, in Wuhan more than 1800 teams of epidemiologists, with a minimum of 5 people/team, are tracing tens of thousands of contacts a day. Contact follow up is painstaking, with a high percentage of identified close contacts completing medical observation. Between 1% and 5% of contacts were subsequently laboratory confirmed cases of COVID-19, depending on location. For example:

- As of 17 February, in Shenzhen City, among 2842 identified close contacts, 2842 (100%) were traced and 2240 (72%) have completed medical observation. Among the close contacts, 88 (2.8%) were found to be infected with COVID-19.

- As of 17 February, in Sichuan Province, among 25493 identified close contacts, 25347 (99%) were traced and 23178 (91%) have completed medical observation. Among the close contacts, 0.9% were found to be infected with COVID-19.
- As of 20 February, in Guangdong Province, among 9939 identified close contacts, 9939 (100%) were traced and 7765 (78%) have completed medical observation. Among the close contacts, 479 (4.8%) were found to be infected with COVID-19.

Testing at fever clinics and from routine ILI/SARI surveillance

The Joint Mission systematically enquired about testing for COVID-19 from routine respiratory disease surveillance systems to explore if COVID-19 is circulating more broadly and undetected in the community in China. These systems could include RT-PCR testing of COVID-19 virus in influenza-like-illness (ILI) and severe acute respiratory infection (SARI) surveillance systems, as well as testing of results among all visitors to fever clinics.

In Wuhan, COVID-19 testing of ILI samples (20 per week) in November and December 2019 and in the first two weeks of January 2020 found no positive results in the 2019 samples, 1 adult positive in the first week of January, and 3 adults positive in the second week of January; all children tested were negative for COVID-19 although a number were positive for influenza. In Guangdong, from 1-14 January, only 1 of more than 15000 ILI/SARI samples tested positive for the COVID-19 virus. In one hospital in Beijing, there were no COVID-19 positive samples among 1910 collected from 28 January 2019 to 13 February 2020. In a hospital in Shenzhen, 0/40 ILI samples were positive for COVID-19.

Within the fever clinics in Guangdong, the percentage of samples that tested positive for the COVID-19 virus has decreased over time from a peak of 0.47% positive on 30 January to 0.02% on 16 February. Overall in Guangdong, 0.14% of approximately 320,000 fever clinic screenings were positive for COVID-19.

Susceptibility

As COVID-19 is a newly identified pathogen, there is no known pre-existing immunity in humans. Based on the epidemiologic characteristics observed so far in China, everyone is assumed to be susceptible, although there may be risk factors increasing susceptibility to infection. This requires further study, as well as to know whether there is neutralising immunity after infection.

The transmission dynamics

Inferring from Figures 2 and 3, and based on our observations at the national and provincial/municipal levels during the Joint Mission, we summarize and interpret the transmission dynamics of COVID-19 thus far. It is important to note that transmission dynamics of any outbreak are inherently contextual. For COVID-19, we observe four major types of transmission dynamics during the epidemic growth phase and in the post-control period, and highlight what is known about transmission in children, as follows:

Transmission in Wuhan

Early cases identified in Wuhan are believed to be have acquired infection from a zoonotic source as many reported visiting or working in the Huanan Wholesale Seafood Market. As of 25 February, an animal source has not yet been identified.

At some point early in the outbreak, some cases generated human-to-human transmission chains that seeded the subsequent community outbreak prior to the implementation of the comprehensive control measures that were rolled out in Wuhan. The dynamics likely approximated mass action and radiated from Wuhan to other parts of Hubei province and China, which explains a relatively high R_0 of 2-2.5.

The *cordon sanitaire* around Wuhan and neighboring municipalities imposed since 23 January 2020 has effectively prevented further exportation of infected individuals to the rest of the country.

Transmission in Hubei, other than Wuhan

In the prefectures immediately adjoining Wuhan (Xiaogan, Huanggang, Jingzhou and Ezhou), transmission is less intense. For other prefectures, due to fewer transport links and human mobility flows with Wuhan, the dynamics are more closely aligned with those observed in the other areas of the country. Within Hubei, the implementation of control measures (including social distancing) has reduced the community force of infection, resulting in the progressively lower incident reported case counts.

Transmission in China outside of Hubei

Given Wuhan's transport hub status and population movement during the Chinese New Year (chunyun), infected individuals quickly spread throughout the country, and were particularly concentrated in cities with the highest volume of traffic with Wuhan. Some of these imported seeds generated limited human-to-human transmission chains at their destination.

Given the Wuhan/Hubei experience, a comprehensive set of interventions, including aggressive case and contact identification, isolation and management and extreme social distancing, have been implemented to interrupt the chains of transmission nationwide. To date, most of the recorded cases were imported from or had direct links to Wuhan/Hubei. Community transmission has been very limited. Most locally generated cases have been clustered, the majority of which have occurred in households, as summarized above.

Of note, the highly clustered nature of local transmission may explain a relatively high R_0 (2-2.5) in the absence of interventions and low confirmed case counts with intense quarantine and social distancing measures.

Special settings

We note that instances of transmission have occurred within health care settings prisons and other closed settings. At the present time, it is not clear what role these settings and groups play in transmission. However, they do not appear to be major drivers of the overall epidemic dynamics. Specifically, we note:

(a) **Transmission in health care settings and among health care workers (HCW)** – The Joint Mission discussed nosocomial infection in all locations visited during the Mission. As of 20 February 2020, there were 2,055 COVID-19 laboratory-confirmed cases reported among HCW from 476 hospitals across China. The majority of HCW cases (88%) were reported from Hubei.

Remarkably, more than 40,000 HCW have been deployed from other areas of China to support the response in Wuhan. Notwithstanding discrete and limited instances of nosocomial outbreaks (e.g. a nosocomial outbreak involving 15 HCW in Wuhan), transmission within health care settings and amongst health care workers does not appear to be a major transmission feature of COVID-19 in China. The Joint Mission learned that, among the HCW infections, most were identified early in the outbreak in Wuhan when supplies and experience with the new disease was lower. Additionally, investigations among HCW suggest that many may have been infected within the household rather than in a health care setting. Outside of Hubei, health care worker infections have been less frequent (i.e. 246 of the total 2055 HCW cases). When exposure was investigated in these limited cases, the exposure for most was reported to have been traced back to a confirmed case in a household.

The Joint Team noted that attention to the prevention of infection in health care workers is of paramount importance in China. Surveillance among health care workers identified factors early in the outbreak that placed HCW at higher risk of infection, and this information has been used to modify policies to improve protection of HCW.

(b) **Transmission in closed settings** – There have been reports of COVID-19 transmission in prisons (Hubei, Shandong, and Zhejiang, China), hospitals (as above) and in a long-term living facility. The close proximity and contact among people in these settings and the potential for environmental contamination are important factors, which could amplify transmission. Transmission in these settings warrants further study.

Children

Data on individuals aged 18 years old and under suggest that there is a relatively low attack rate in this age group (2.4% of all reported cases). Within Wuhan, among testing of ILI samples, no children were positive in November and December of 2019 and in the first two weeks of January 2020. From available data, and in the absence of results from serologic studies, it is not possible to determine the extent of infection among children, what role children play in transmission, whether children are less susceptible or if they present differently clinically (i.e. generally milder presentations). The Joint Mission learned that infected children have largely been identified through contact tracing in households of adults. Of note, people interviewed by the Joint Mission Team could not recall episodes in which transmission occurred from a child to an adult.

The signs, symptoms, disease progression and severity

Symptoms of COVID-19 are non-specific and the disease presentation can range from no symptoms (asymptomatic) to severe pneumonia and death. As of 20 February 2020 and

based on 55924 laboratory confirmed cases, typical **signs and symptoms** include: fever (87.9%), dry cough (67.7%), fatigue (38.1%), sputum production (33.4%), shortness of breath (18.6%), sore throat (13.9%), headache (13.6%), myalgia or arthralgia (14.8%), chills (11.4%), nausea or vomiting (5.0%), nasal congestion (4.8%), diarrhea (3.7%), and hemoptysis (0.9%), and conjunctival congestion (0.8%).

People with COVID-19 generally develop signs and symptoms, including mild respiratory symptoms and fever, on an average of 5-6 days after infection (mean incubation period 5-6 days, range 1-14 days).

Most people infected with COVID-19 virus have mild disease and recover. Approximately 80% of laboratory confirmed patients have had **mild to moderate disease**, which includes non-pneumonia and pneumonia cases, 13.8% have **severe disease** (dyspnea, respiratory frequency ≥30/minute, blood oxygen saturation ≤93%, PaO2/FiO2 ratio <300, and/or lung infiltrates >50% of the lung field within 24-48 hours) and 6.1% are **critical** (respiratory failure, septic shock, and/or multiple organ dysfunction/failure). **Asymptomatic infection** has been reported, but the majority of the relatively rare cases who are asymptomatic on the date of identification/report went on to develop disease. The proportion of truly asymptomatic infections is unclear but appears to be relatively rare and does not appear to be a major driver of transmission.

Individuals at **highest risk** for severe disease and death include people aged over 60 years and those with underlying conditions such as hypertension, diabetes, cardiovascular disease, chronic respiratory disease and cancer. Disease in **children** appears to be relatively rare and mild with approximately 2.4% of the total reported cases reported amongst individuals aged under 19 years. A very small proportion of those aged under 19 years have developed severe (2.5%) or critical disease (0.2%).

As of 20 February, 2114 of the 55,924 laboratory confirmed cases have died (**crude fatality ratio** [CFR[2]] 3.8%) (note: at least some of whom were identified using a case definition that included pulmonary disease). The overall CFR varies by location and intensity of transmission (i.e. 5.8% in Wuhan vs. 0.7% in other areas in China). In China, the overall CFR was higher in the early stages of the outbreak (17.3% for cases with symptom onset from 1-10 January) and has reduced over time to 0.7% for patients with symptom onset after 1 February (Figure 4). The Joint Mission noted that the standard of care has evolved over the course of the outbreak.

Mortality increases with age, with the highest mortality among people over 80 years of age (CFR 21.9%). The CFR is higher among males compared to females (4.7% vs. 2.8%). By occupation, patients who reported being retirees had the highest CFR at 8.9%. While patients who reported no comorbid conditions had a CFR of 1.4%, patients with comorbid conditions had much higher rates: 13.2% for those with cardiovascular disease, 9.2% for diabetes, 8.4% for hypertension, 8.0% for chronic respiratory disease, and 7.6% for cancer.

[2] The Joint Mission acknowledges the known challenges and biases of reporting crude CFR early in an epidemic.

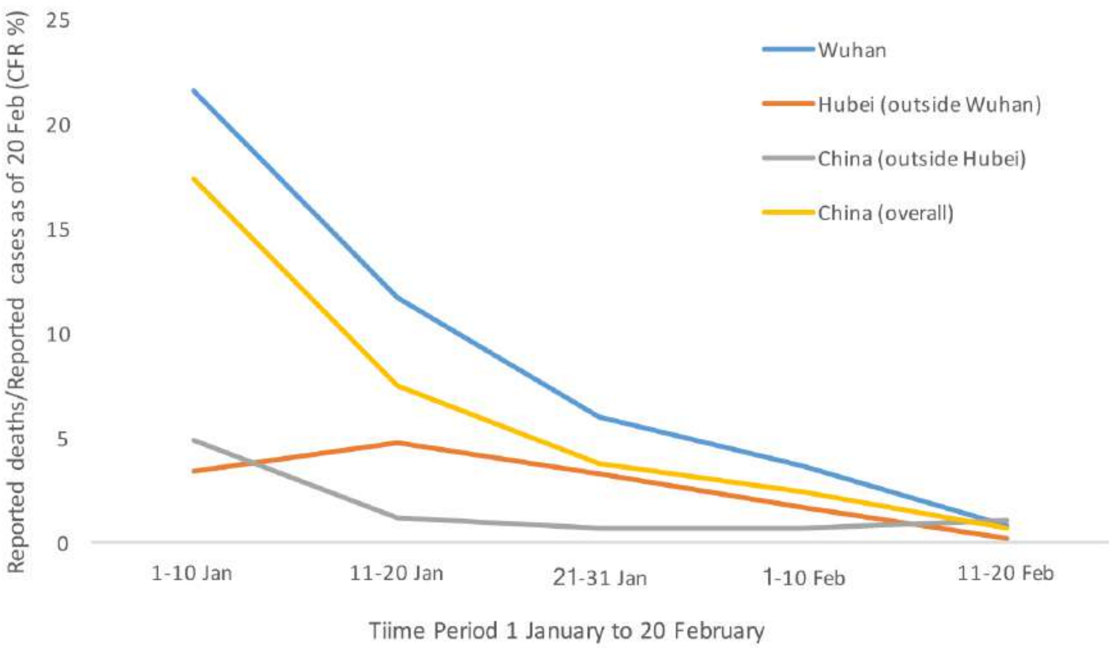


Figure 4 Case fatality ratio (reported deaths among total cases) for COVID-19 in China over time and by location, as of 20 February 2020

Data on the **progression of disease** is available from a limited number of reported hospitalized cases (Figure 5). Based on available information, the median time from symptom onset to laboratory confirmation nationally decreased from 12 days (range 8-18 days) in early January to 3 days (1-7) by early February 2020, and in Wuhan from 15 days (10-21) to 5 days (3-9), respectively. This has allowed for earlier case and contact identification, isolation and treatment.

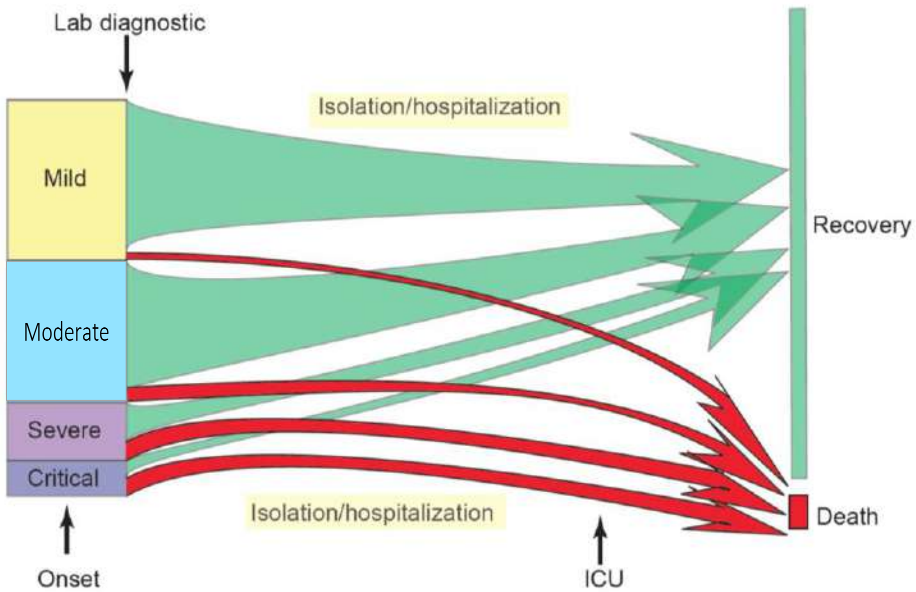


Figure 5. Pattern of disease progression for COVID-19 in China

Note: the relative size of the boxes for disease severity and outcome reflect the proportion of cases reported as of 20 February 2020. The size of the arrows indicates the proportion of cases who recovered or died. Disease definitions are described above. Moderate cases have a mild form of pneumonia.

Using available preliminary data, the median time from onset to clinical recovery for mild cases is approximately 2 weeks and is 3-6 weeks for patients with severe or critical disease. Preliminary data suggests that the time period from onset to the development of severe disease, including hypoxia, is 1 week. Among patients who have died, the time from symptom onset to outcome ranges from 2-8 weeks.

An increasing number of patients have **recovered**; as of 20 February, 18264 (24%) reported cases have recovered. Encouragingly, a report on 20 February from the Guangdong CDC suggests that of 125 severe cases identified in Guangdong, 33 (26.4%) have recovered and been released from hospital, and 58 (46.4%) had improved and were reclassified as having mild/moderate disease (i.e. + milder pneumonia). Among severe cases reported to date, 13.4% have died. Early identification of cases and contacts allows for earlier treatment.

The China response

Upon the detection of a cluster of pneumonia cases of unknown etiology in Wuhan, the CPC Central Committee and the State Council launched the national emergency response. A **Central Leadership Group for Epidemic Response** and the **Joint Prevention and Control Mechanism** of the State Council were established. General Secretary Xi Jinping personally directed and deployed the prevention and control work and requested that the prevention and control of the COVID-19 outbreak be the top priority of government at all levels. Prime Minister Li Keqiang headed the Central Leading Group for Epidemic Response and went to Wuhan to inspect and coordinate the prevention and control work of relevant departments and provinces (autonomous regions and municipalities) across the country. Vice Premier Sun Chunlan, who has been working on the frontlines in Wuhan, has led and coordinated the frontline prevention and control of the outbreak.

The prevention and control measures have been implemented rapidly, from the early stages in Wuhan and other key areas of Hubei, to the current overall national epidemic. It has been undertaken in **three main phases**, with two important events defining those phases. First, COVID-19 was included in the statutory report of Class B infectious diseases and border health quarantine infectious diseases on 20 January 2020, which marked the transition from the initial partial control approach to the comprehensive adoption of various control measures in accordance with the law. The second event was the State Council's issuing, on 8 February 2020, of The Notice on Orderly Resuming Production and Resuming Production in Enterprises, which indicated that China's national epidemic control work had entered a stage of overall epidemic prevention and control together with the restoration of normal social and economic operations.

The first stage

During the early stage of the outbreak, the main strategy focused on preventing the exportation of cases from Wuhan and other priority areas of Hubei Province, and preventing the importation of cases by other provinces; the overall aim was to control the source of infection, block transmission and prevent further spread. The response mechanism was initiated with multi-sectoral involvement in joint prevention and control measures. Wet markets were closed, and efforts were made to identify the zoonotic source. Information on the epidemic was notified to WHO on 3 January, and whole genome sequences of the COVID-19 virus were shared with WHO on 10 January. Protocols for COVID-19 diagnosis and

treatment, surveillance, epidemiological investigation, management of close contacts, and laboratory testing were formulated, and relevant surveillance activities and epidemiological investigations conducted. Diagnostic testing kits were developed, and wildlife and live poultry markets were placed under strict supervision and control measures.

The second stage

During the second stage of the outbreak, the main strategy was to reduce the intensity of the epidemic and to slow down the increase in cases. In Wuhan and other priority areas of Hubei Province, the focus was on actively treating patients, reducing deaths, and preventing exportations. In other provinces, the focus was on preventing importations, curbing the spread of the disease and implementing joint prevention and control measures. Nationally, wildlife markets were closed and wildlife captive-breeding facilities were cordoned off. On 20 January, COVID-19 was included in the notifiable report of Class B infectious diseases and border health quarantine infectious diseases, with temperature checks, health care declarations, and quarantine against COVID-19 instituted at transportation depots in accordance with the law. On 23 January, Wuhan implemented strict traffic restrictions. The protocols for diagnosis, treatment and epidemic prevention and control were improved; case isolation and treatment were strengthened.

Measures were taken to ensure that all cases were treated, and close contacts were isolated and put under medical observation. Other measures implemented included the extension of the Spring Festival holiday, traffic controls, and the control of transportation capacity to reduce the movement of people; mass gathering activities were also cancelled. Information about the epidemic and prevention and control measures was regularly released. Public risk communications and health education were strengthened; allocation of medical supplies was coordinated, new hospitals were built, reserve beds were used and relevant premises were repurposed to ensure that all cases could be treated; efforts were made to maintain a stable supply of commodities and their prices to ensure the smooth operation of society.

The third stage

The third stage of the outbreak focused on reducing clusters of cases, thoroughly controlling the epidemic, and striking a balance between epidemic prevention and control, sustainable economic and social development, the unified command, standardized guidance, and scientific evidence-based policy implementation. For Wuhan and other priority areas of Hubei Province, the focus was on patient treatment and the interruption of transmission, with an emphasis on concrete steps to fully implement relevant measures for the testing, admitting and treating of all patients. A risk-based prevention and control approach was adopted with differentiated prevention and control measures for different regions of the country and provinces. Relevant measures were strengthened in the areas of epidemiological investigation, case management and epidemic prevention in high-risk public places.

New technologies were applied such as the use of big data and artificial intelligence (AI) to strengthen contact tracing and the management of priority populations. Relevant health insurance policies were promulgated on "health insurance payment, off-site settlement, and financial compensation". All provinces provided support to Wuhan and priority areas in Hubei Province in an effort to quickly curb the spread of the disease and provide timely clinical treatment. Pre-school preparation was improved, and work resumed in phases and

batches. Health and welfare services were provided to returning workers in a targeted and 'one-stop' manner. Normal social operations are being restored in a stepwise fashion; knowledge about disease prevention is being popularized to improve public health literacy and skills; and a comprehensive program of emergency scientific research is being carried out to develop diagnostics, therapeutics and vaccines, delineate the spectrum of the disease, and identify the source of the virus.

Knowledge gaps

Since the start of the COVID-19 outbreak, there have been extensive attempts to better understand the virus and the disease in China. It is remarkable how much knowledge about a new virus has been gained in such a short time. However, as with all new diseases, and only 7 weeks after this outbreak began, key knowledge gaps remain. Annex D summarizes the key unknowns in a number of areas including the source of infection, pathogenesis and virulence of the virus, transmissibility, risk factors for infection and disease progression, surveillance, diagnostics, clinical management of severe and critically ill patients, and the effectiveness of prevention and control measures. The timely filling of these knowledge gaps is imperative to enhance control strategies.

III. Assessment

The Joint Mission drew four major conclusions from its work in China and four major conclusions from its knowledge of the broader global response to COVID-19. Recommendations are offered in five major areas to inform the ongoing response globally and in China.

The China Response & Next Steps

1. **In the face of a previously unknown virus, China has rolled out perhaps the most ambitious, agile and aggressive disease containment effort in history. The strategy that underpinned this containment effort was initially a national approach that promoted universal temperature monitoring, masking, and hand washing. However, as the outbreak evolved, and knowledge was gained, a science and risk-based approach was taken to tailor implementation. Specific containment measures were adjusted to the provincial, county and even community context, the capacity of the setting, and the nature of novel coronavirus transmission there.**

   While the fundamental principles of this strategy have been consistent since its launch, there has been constant refinement of specific aspects to incorporate new knowledge on the novel coronavirus, the COVID-19 disease, and COVID-19 containment, as rapidly as that knowledge has emerged. The remarkable speed with which Chinese scientists and public health experts isolated the causative virus, established diagnostic tools, and determined key transmission parameters, such as the route of spread and incubation period, provided the vital evidence base for China's strategy, gaining invaluable time for the response.

As striking, has been the uncompromising rigor of strategy application that proved to be a hallmark in every setting and context where it was examined. There has also been a relentless focus on improving key performance indicators, for example constantly enhancing the speed of case detection, isolation and early treatment. The implementation of these containment measures has been supported and enabled by the innovative and aggressive use of cutting edge technologies, from shifting to online medical platforms for routine care and schooling, to the use of 5G platforms to support rural response operations.

2. **Achieving China's exceptional coverage with and adherence to these containment measures has only been possible due to the deep commitment of the Chinese people to collective action in the face of this common threat. At a community level this is reflected in the remarkable solidarity of provinces and cities in support of the most vulnerable populations and communities. Despite ongoing outbreaks in their own areas, Governors and Mayors have continued to send thousands of health care workers and tons of vital PPE supplies into Hubei province and Wuhan city.**

   At the individual level, the Chinese people have reacted to this outbreak with courage and conviction. They have accepted and adhered to the starkest of containment measures – whether the suspension of public gatherings, the month-long 'stay at home' advisories or prohibitions on travel. Throughout an intensive 9-days of site visits across China, in frank discussions from the level of local community mobilizers and frontline health care providers to top scientists, Governors and Mayors, the Joint Mission was struck by the sincerity and dedication that each brings to this COVID-19 response.

3. **China's bold approach to contain the rapid spread of this new respiratory pathogen has changed the course of a rapidly escalating and deadly epidemic. A particularly compelling statistic is that on the first day of the advance team's work there were 2478 newly confirmed cases of COVID-19 reported in China. Two weeks later, on the final day of this Mission, China reported 409 newly confirmed cases. This decline in COVID-19 cases across China is real.**

   Several sources of data support this conclusion, including the steep decline in fever clinic visits, the opening up of treatment beds as cured patients are discharged, and the challenges to recruiting new patients for clinical trials. Based on a comparison of crude attack rates across provinces, the Joint Mission estimates that this truly all-of-Government and all-of-society approach that has been taken in China has averted or at least delayed hundreds of thousands of COVID-19 cases in the country. By extension, the reduction that has been achieved in the force of COVID-19 infection in China has also played a significant role in protecting the global community and creating a stronger first line of defense against international spread. Containing this outbreak, however, has come at great cost and sacrifice by China and its people, in both human and material terms.

   While the scale and impact of China's COVID-19 operation has been remarkable, it has also highlighted areas for improvement in public health emergency response capacity.

These include overcoming any obstacles to act immediately on early alerts, to massively scale-up capacity for isolation and care, to optimize the protection of frontline health care workers in all settings, to enhance collaborative action on priority gaps in knowledge and tools, and to more clearly communicate key data and developments internationally.

4. **China is already, and rightfully, working to bolster its economy, reopen its schools and return to a more normal semblance of its society, even as it works to contain the remaining chains of COVID-19 transmission. Appropriately, a science-based, risk-informed and phased approach is being taken, with a clear recognition and readiness of the need to immediately react to any new COVID-19 cases or clusters as key elements of the containment strategy are lifted.**

   Despite the declining case numbers, across China every province, city and community visited is urgently escalating their investments in acute care beds and public health capacity. It is crucial that this continues. Fifty thousand infected COVID-19 patient are still under treatment, across the country. However, the Joint Mission has come to understand the substantial knowledge, experience and capacities that China has rapidly built during this crisis. Consequently, it endorses China's working assumption that in most provinces and municipalities it should soon be possible to manage a resurgence in COVID-19 cases, using even more tailored and sustainable approaches that are anchored in very rapid case detection, instant activation of key containment activities, direct oversight by top leadership, and broad community engagement.

   As China works to resume a more normal level of societal and economic activity, it is essential that the world recognizes and reacts positively to the rapidly changing, and decreasing, risk of COVID-19 in the country. China's rapid return to full connectivity with the world, and to full productivity and economic output, is vital to China and to the world. The world urgently needs access to China's experience in responding to COVID-19, as well as the material goods it brings to the global response. It is even more urgent now, with escalating COVID-19 outbreaks outside of China, to constantly reassess any restrictions on travel and/or trade to China that go beyond the recommendations of the IHR Emergency Committee on COVID-19.

The Global Response & Next Steps

1. **The COVID-19 virus is a new pathogen that is highly contagious, can spread quickly, and must be considered capable of causing enormous health, economic and societal impacts in any setting. It is not SARS and it is not influenza. Building scenarios and strategies only on the basis of well-known pathogens risks failing to exploit all possible measures to slow transmission of the COVID-19 virus, reduce disease and save lives.**

   COVID-19 is not SARS and it is not influenza. It is a new virus with its own characteristics. For example, COVID-19 transmission in children appears to be limited compared with influenza, while the clinical picture differs from SARS. Such differences, while based on limited data, may be playing a role in the apparent efficacy of rigorously

applied non-pharmaceutical, public health measures to interrupt chains of human-to-human transmission in a range of settings in China. The COVID-19 virus is unique among human coronaviruses in its combination of high transmissibility, substantial fatal outcomes in some high-risk groups, and ability to cause huge societal and economic disruption. For planning purposes, it must be assumed that the global population is susceptible to this virus. As the animal origin of the COVID-19 virus is unknown at present, the risk of reintroduction into previously infected areas must be constantly considered.

The novel nature, and our continuously evolving understanding, of this coronavirus demands a tremendous agility in our capacity to rapidly adapt and change our readiness and response planning as has been done continually in China. This is an extraordinary feat for a country of 1.4 billion people.

2. **China's uncompromising and rigorous use of non-pharmaceutical measures to contain transmission of the COVID-19 virus in multiple settings provides vital lessons for the global response. This rather unique and unprecedented public health response in China reversed the escalating cases in both Hubei, where there has been widespread community transmission, and in the importation provinces, where family clusters appear to have driven the outbreak.**

   Although the timing of the outbreak in China has been relatively similar across the country, transmission chains were established in a wide diversity of settings, from mega-cities in the north and south of the country, to remote communities. However, the rapid adaptation and tailoring of China's strategy demonstrated that containment can be adapted and successfully operationalized in a wide range of settings.

   China's experience strongly supports the efficacy and effectiveness of anchoring COVID-19 readiness and rapid response plans in a thorough assessment of local risks and of utilizing a differentiated risk-based containment strategy to manage the outbreak in areas with no cases vs. sporadic cases vs. clusters of cases vs. community-level transmission. Such a strategy is essential for ensuring a sustainable approach while minimizing the socio-economic impact.

3. **Much of the global community is not yet ready, in mindset and materially, to implement the measures that have been employed to contain COVID-19 in China. These are the only measures that are currently proven to interrupt or minimize transmission chains in humans. Fundamental to these measures is extremely proactive surveillance to immediately detect cases, very rapid diagnosis and immediate case isolation, rigorous tracking and quarantine of close contacts, and an exceptionally high degree of population understanding and acceptance of these measures.**

   Achieving the high quality of implementation needed to be successful with such measures requires an unusual and unprecedented speed of decision-making by top leaders, operational thoroughness by public health systems, and engagement of society.

Given the damage that can be caused by uncontrolled, community-level transmission of this virus, such an approach is warranted to save lives and to gain the weeks and months needed for the testing of therapeutics and vaccine development. Furthermore, as the majority of new cases outside of China are currently occurring in high and middle-income countries, a rigorous commitment to slowing transmission in such settings with non-pharmaceutical measures is vital to achieving a second line of defense to protect low income countries that have weaker health systems and coping capacities.

The time that can be gained through the full application of these measures – even if just days or weeks – can be invaluable in ultimately reducing COVID-19 illness and deaths. This is apparent in the huge increase in knowledge, approaches and even tools that has taken place in just the 7 weeks since this virus was discovered through the rapid scientific work that has been done in China.

4. **The time gained by rigorously applying COVID-19 containment measures must be used more effectively to urgently enhance global readiness and rapidly develop the specific tools that are needed to ultimately stop this virus.**

   COVID-19 is spreading with astonishing speed; COVID-19 outbreaks in any setting have very serious consequences; and there is now strong evidence that non-pharmaceutical interventions can reduce and even interrupt transmission. Concerningly, global and national preparedness planning is often ambivalent about such interventions. However, to reduce COVID-19 illness and death, near-term readiness planning must embrace the large-scale implementation of high-quality, non-pharmaceutical public health measures. These measures must fully incorporate immediate case detection and isolation, rigorous close contact tracing and monitoring/quarantine, and direct population/community engagement.

   A huge array of COVID-19 studies, scientific research projects and product R&D efforts are ongoing in China and globally. This is essential and to be encouraged and supported. However, such a large number of projects and products needs to be prioritized. Without prioritizing, this risks compromising the concentration of attention and resources and collaboration required to cut timelines by precious weeks and months. While progress has been made, the urgency of the COVID-19 situation supports an even more ruthless prioritization of research in the areas of diagnostics, therapeutics and vaccines.

   Similarly, there is a long list of proposed studies on the origins of COVID-19, the natural history of the disease, and the virus's transmission dynamics. However, the urgency of responding to cases and saving lives makes it difficult for policy makers to consider and act on such comprehensive lists. This can be addressed by balancing studies with the immediate public health and clinical needs of the response. Studies can be prioritized in terms of the largest knowledge gaps that can be most rapidly addressed to have greatest immediate impact on response operations and patient management. This suggests prioritizing studies to identify risk factors for transmission in households, institutions and the community; convenience sampling for this virus in the population using existing surveillance systems; age-stratified sero-epidemiologic surveys; the analysis of clinical case series; and cluster investigations.

IV. Major Recommendations

For China

1. Maintain an appropriate level of emergency management protocols, depending on the assessed risk in each area and recognizing the real risk of new cases and clusters of COVID-19 as economic activity resumes, movement restrictions are lifted, and schools reopen;

2. Carefully monitor the phased lifting of the current restrictions on movement and public gatherings, beginning with the return of workers and migrant labor, followed by the eventual reopening of schools and lifting other measures;

3. Further strengthen the readiness of emergency management mechanisms, public health institutions (e.g. CDCs), medical facilities, and community engagement mechanisms to ensure sustained capacity to immediately launch containment activities in response to any resurgence in cases;

4. Prioritize research that rapidly informs response and risk management decisions, particularly household and health care facility studies, age-stratified sero-epidemiologic surveys and rigorous investigation of the animal-human interface; establish a centralized research program to fast-track the most promising rapid diagnostics and serologic assays, the testing of potential antivirals and vaccine candidates, and Chinese engagement in selected multi-country trials; and

5. As the country with the greatest knowledge on COVID-19, further enhance the systematic and real-time sharing of epidemiologic data, clinical results and experience to inform the global response.

For countries with imported cases and/or outbreaks of COVID-19

1. Immediately activate the highest level of national Response Management protocols to ensure the all-of-government and all-of-society approach needed to contain COVID-19 with non-pharmaceutical public health measures;

2. Prioritize active, exhaustive case finding and immediate testing and isolation, painstaking contact tracing and rigorous quarantine of close contacts;

3. Fully educate the general public on the seriousness of COVID-19 and their role in preventing its spread;

4. Immediately expand surveillance to detect COVID-19 transmission chains, by testing all patients with atypical pneumonias, conducting screening in some patients with upper respiratory illnesses and/or recent COVID-19 exposure, and adding testing for the COVID-19 virus to existing surveillance systems (e.g. systems for influenza-like-illness and SARI); and

5. Conduct multi-sector scenario planning and simulations for the deployment of even more stringent measures to interrupt transmission chains as needed (e.g. the suspension of large-scale gatherings and the closure of schools and workplaces).

For uninfected countries

1. Prepare to immediately activate the highest level of emergency response mechanisms to trigger the all-of-government and all-of society approach that is essential for early containment of a COVID-19 outbreak;

2. Rapidly test national preparedness plans in light of new knowledge on the effectiveness of non-pharmaceutical measures against COVID-19; incorporate rapid detection, largescale case isolation and respiratory support capacities, and rigorous contact tracing and management in national COVID-19 readiness and response plans and capacities;

3. Immediately enhance surveillance for COVID-19 as rapid detection is crucial to containing spread; consider testing all patients with atypical pneumonia for the COVID-19 virus, and adding testing for the virus to existing influenza surveillance systems;

4. Begin now to enforce rigorous application of infection prevention and control measures in all healthcare facilities, especially in emergency departments and outpatient clinics, as this is where COVID-19 will enter the health system; and

5. Rapidly assess the general population's understanding of COVID-19, adjust national health promotion materials and activities accordingly, and engage clinical champions to communicate with the media.

For the public

1. Recognize that COVID-19 is a new and concerning disease, but that outbreaks can managed with the right response and that the vast majority of infected people will recover;

2. Begin now to adopt and rigorously practice the most important preventive measures for COVID-19 by frequent hand washing and always covering your mouth and nose when sneezing or coughing;

3. Continually update yourself on COVID-19 and its signs and symptoms (i.e. fever and dry cough), because the strategies and response activities will constantly improve as new information on this disease is accumulating every day; and

4. Be prepared to actively support a response to COVID-19 in a variety of ways, including the adoption of more stringent 'social distancing' practices and helping the high-risk elderly population.

For the international community

1. Recognize that true solidarity and collaboration is essential between nations to tackle the common threat that COVID-19 represents and operationalize this principle;

2. Rapidly share information as required under the International Health Regulations (IHR) including detailed information about imported cases to facilitate contact tracing and inform containment measures that span countries;

3. Recognize the rapidly changing risk profile of COVID-19 affected countries and continually monitor outbreak trends and control capacities to reassess any 'additional health measures' that significantly interfere with international travel and trade.

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Annexes

A. WHO-China Joint Mission Members

Bruce AYLWARD	Team Lead WHO-China Joint Mission on COVID-19, Senior Advisor to the Director-General, World Health Organization, Geneva, Switzerland
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Zhongze WU	Director, Compliance and Enforcement Division, Department of Wildlife Conservation, National Forestry and Grassland Administration
Zunyou WU	Chief Epidemiologist, Chinese Center for Disease Control and Prevention
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Weigong ZHOU	Medical Officer, Influenza Division, National Center for Immunization and Respiratory Diseases, US Centers for Disease Control and Prevention, Atlanta, United States
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Lei ZHOU	Chief and Researcher, Branch for Emerging Infectious Disease, Public Health Emergency Center, Chinese Center for Disease Control and Prevention

B. Summary Agenda of the Mission

Dates	Location	Activities
10-15 February 2020 (Advance Team)	Beijing	Advance Team and WHO Country team meetings with national counterparts and institutions
16 February 2020	Beijing	Meeting with the full international team for briefing at the WHO Country office
	Beijing	Workshop at the National Health Commission (NHC) with relevant departments of the Joint Prevention and Control Mechanism of the State Council
17 February 2020	Beijing	Site visit to Beijing Ditan Hospital
	Beijing	Site visit to Anhuali community and health service station, Anzhen street, Chaoyang District, Beijing
	Beijing	Workshop with Chinese Center for Disease Control and Prevention
18 February 2020 (Guangdong Team)	Shenzhen, Guangdong	Shenzhen customs at the airport
	Shenzhen, Guangdong	Shenzhen No.3 People's Hospital
	Shenzhen, Guangdong	Shenzhen Center for Disease Control and Prevention
	Shenzhen, Guangdong	Meeting at Tencent
19 February 2020 (Guangdong Team)	Shenzhen, Guangdong	Qiaoxiang community
	Shenzhen to Guangzhou	Visit to Futian High-speed Train Station, and travel to Guangzhou by train
	Guangzhou	Guangzhou Panyu Sanatorium
	Guangzhou	Guangdong Laboratory of Regenerative Medicine and Health
	Guangzhou	Guangzhou Tiyudongzhihui wet market
	Guangzhou	First Workshop with The People's government of Guangdong Province
20 February 2020 (Guangdong Team)	Guangzhou	Guangdong Provincial Center for Disease Control and Prevention
	Guangzhou	Renmin road campus of Guangzhou Women and Children Medical Center
	Guangzhou	The second Workshop with The People's government of Guangdong Province
18 February 2020 (Sichuan Team)	Beijing to Chengdu	
	Sichuan	Site visit to Chengdu Shuangliu International Airport
		Meeting with the Governor of Sichuan Provincial People's Government
		Site visit to Yong'an Township Central hospital with fever clinic
		Site visit to home community of Yong'an township
19 February 2020 (Sichuan Team)		Symposium with provincial and municipal authorities
		Sichuan Center for Disease Control and Prevention
		Site visit to West China Hospital- Designated COVID-19 hospital
20 February 2020 (Sichuan Team)		Site visit to Chengdu Women and Children's hospital
		Site visit to Pharmaceutical Logistics center
		Site visit to East Chengdu railway station

		Site visit to Chengdu Public Health Clinical Centre- Designated COVID 19 hospital
Sichuan and Guangdong teams reconvene in Guangzhou		
21-24 February 2020		Analyze major findings; Meetings of the WHO-China Joint mission to finalize the report
Feb 22 (Wuhan Team)	Guangzhou to Wuhan	Select team members only
23 February (Wuhan Team)		Site visit to Guanggu Campus of Wuhan Tongji Hospital
		Site visit to Mobile Cabin Hospital in Wuhan Sports Center
		Workshop with relevant departments of the Joint Prevention and Control Mechanism of Hubei Province
		Feedback Meeting with Minister Ma, NHC at the Wuhan Conference Center
24 February 2020	Guangzhou to Beijing	Finalize report, WHO-Joint Press conference in Beijing

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C. Detailed Technical Findings

Response management, case and contact management, risk communication and community engagement

The response structures in China were rapidly put in place according to existing emergency plans and aligned from the top to the bottom. This was replicated at the four levels of government (national provincial, prefecture and county/district).

Organizational structure and response mechanism

Response activation at the national level: COVID-19 prevention and control mechanisms were initiated immediately after the outbreak was declared and nine working groups were set up to coordinate the response: a) Coordination b) Epidemic prevention and control c) Medical treatment d) Research e) Public communication f) Foreign affairs g) Medical material support h) Life maintenance supplies and i) Social stability. Each working group has a ministerial level leader. Emergency response laws and regulations for the emergency response to public health emergencies, prevention and control of infectious diseases have been developed or updated to guide the response.

Response activation in provinces: Each province set up a similar structure to manage the outbreak. The response is organized at the levels of national, provincial, prefecture, county/district and the community. By 29 January, all provinces across China had launched the highest level of response for major public health emergencies.

Response Strategy

A clear strategy was developed, and goals were well articulated and communicated across the entire response architecture. This strategy was rapidly adapted and adjusted to the outbreak, both in terms of the epidemiological situation over time and in different parts of the country.

The epidemiological situation has been used to define location into four areas:

- In areas without cases, the strategy in these areas is to "strictly prevent introduction". This includes quarantine arrangements in transportation hubs, monitoring for temperature changes, strengthening of triage arrangements, use of fever clinics, and ensuring normal economic and social operations.
- In areas with sporadic cases, the strategy is focused on "reducing importation, stopping transmission and providing appropriate treatment".
- In areas with community clusters, the strategy is focussed on "stopping transmission, preventing exportation, and strengthening treatment".
- In areas with community transmission, the strictest prevention and control strategies are being implemented, the entry and exit of people from these areas has been stopped and public health and medical treatment measures are comprehensively strengthened.

Main control measures implemented in China

The main control measures implemented in China are as follows and are illustrated in Figures 6A-6D, representing the national level response and examples of the response at the Provincial and municipal levels:

Monitoring and reporting: COVID-19 was included in the statutory reporting of infectious diseases on 20 January and plans were formulated to strengthen diagnosis, monitoring, and reporting.

Strengthening ports of entry and quarantine: The Customs Department launched the emergency plan for public health emergencies at ports across the country and restarted the health declaration card system for entry and exit into cities as well as strict monitoring of the temperature of entry and exit passengers.

Treatment: For severe or critical patients, the principle of "Four Concentrations" was implemented: i.e. concentrating patients, medical experts, resources and treatment into special centres. All cities and districts transformed relevant hospitals, increased the number of designated hospitals, dispatched medical staff, and set up expert groups for consultation, so as to minimise mortality of severe patients. Medical resources from all over China have been mobilized to support the medical treatment of patients in Wuhan.

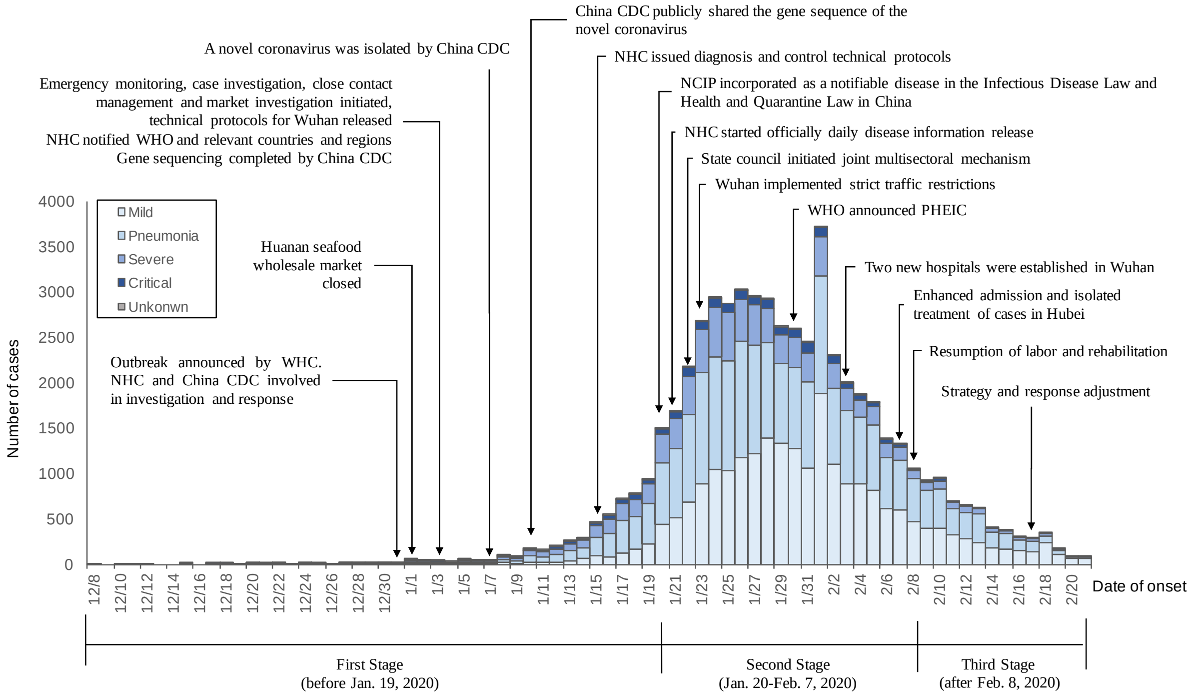
Epidemiological investigation and close contact management: Strong epidemiological investigations are being carried out for cases, clusters, and contacts to identify the source of infection and implement targeted control measures, such as contact tracing.

Social distancing: At the national level, the State Council extended the Spring Festival holiday in 2020, all parts of the country actively cancelled or suspended activities like sport events, cinema, theatre, and schools and colleges in all parts of the country postponed re-opening after the holiday. Enterprises and institutions have staggered their return to work. Transportation Departments setup thousands of health and quarantine stations in national service areas, and in entrances and exits for passengers at stations. Hubei Province adopted the most stringent traffic control measures, such as suspension of urban public transport, including subway, ferry and long-distance passenger transport. Every citizen has to wear a mask in public. Home support mechanisms were established. As a consequence of all of these measures, public life is very reduced.

Funding and material support: Payment of health insurance was taken over by the state, as well as the work to improve accessibility and affordability of medical materials, provide personal protection materials, and ensure basic living materials for affected people.

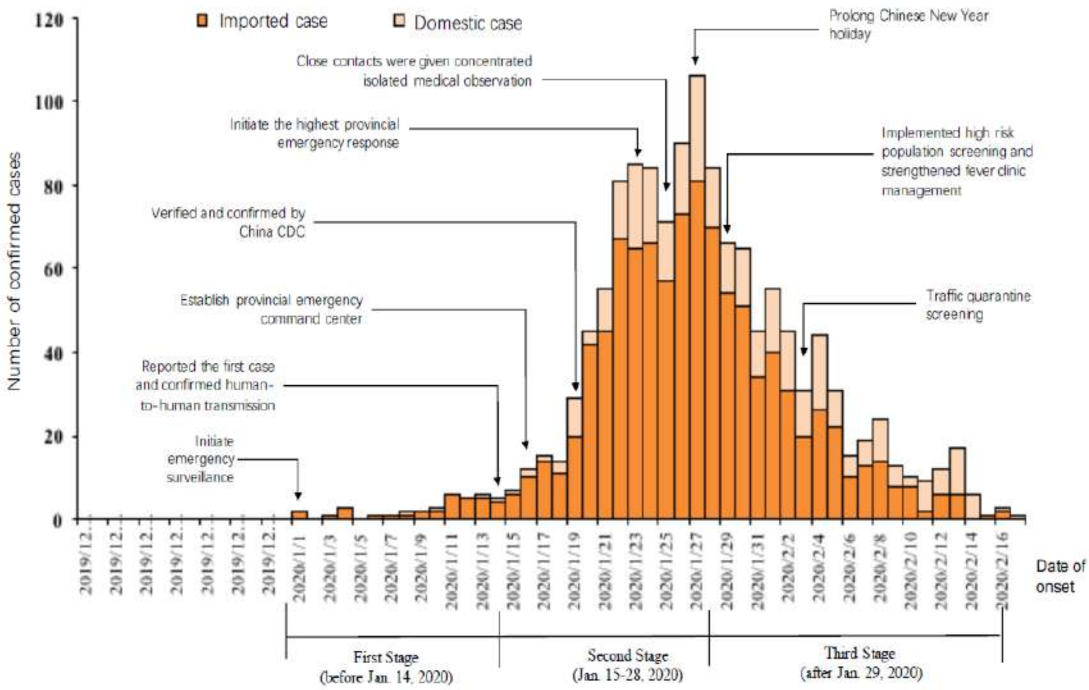
Emergency material support: The government restored production and expanded production capacity, organized key enterprises that have already started to exceed current production capacity, supported local enterprises to expand imports, and used cross-border e-commerce platforms and enterprises to help import medical materials and improve the ability to guarantee supplies.

A



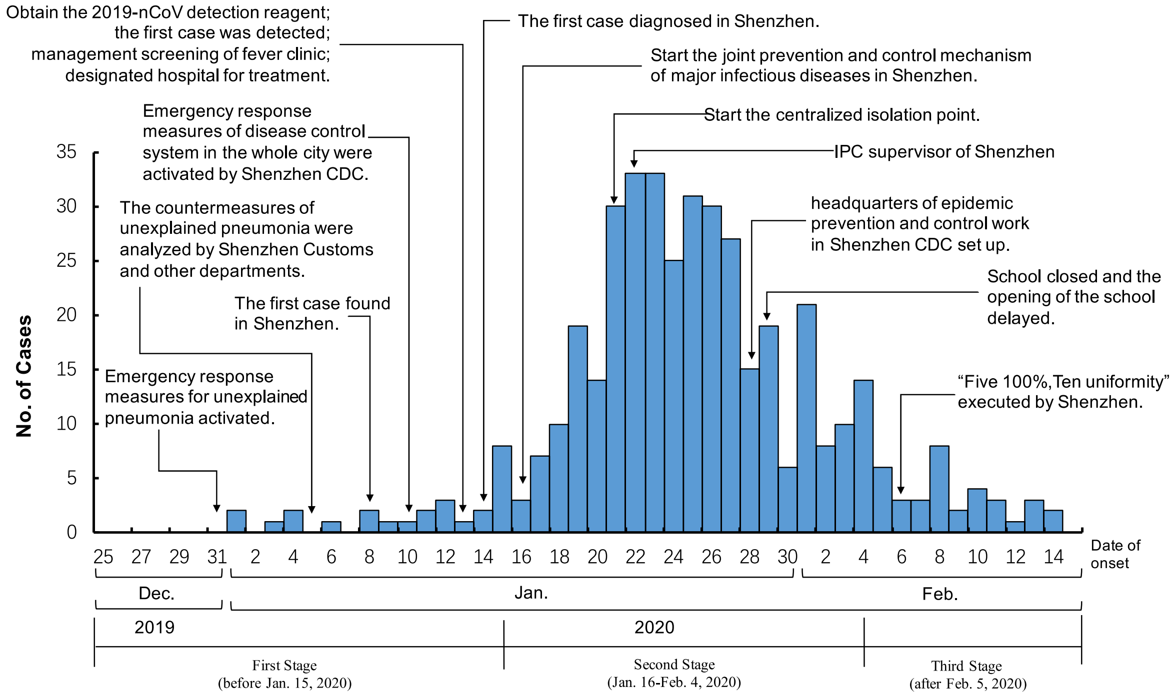
China CDC publicly shared the gene sequence of the novel coronavirus
A novel coronavirus was isolated by China CDC
NHC issued diagnosis and control technical protocols
Emergency monitoring, case investigation, close contact management and market investigation initiated, technical protocols for Wuhan released
NHC notified WHO and relevant countries and regions
Gene sequencing completed by China CDC
NCIP incorporated as a notifiable disease in the Infectious Disease Law and Health and Quarantine Law in China
NHC started officially daily disease information release
State council initiated joint multisectoral mechanism
Wuhan implemented strict traffic restrictions
WHO announced PHEIC
Two new hospitals were established in Wuhan
Enhanced admission and isolated treatment of cases in Hubei
Resumption of labor and rehabilitation
Strategy and response adjustment
Huanan seafood wholesale market closed
Outbreak announced by WHC. NHC and China CDC involved in investigation and response
Mild
Pneumonia
Severe
Critical
Unkonwn
Number of cases
Date of onset
First Stage (before Jan. 19, 2020)
Second Stage (Jan. 20-Feb. 7, 2020)
Third Stage (after Feb. 8, 2020)

B



Imported case
Domestic case
Prolong Chinese New Year holiday
Close contacts were given concentrated isolated medical observation
Initiate the highest provincial emergency response
Implemented high risk population screening and strengthened fever clinic management
Verified and confirmed by China CDC
Establish provincial emergency command center
Traffic quarantine screening
Reported the first case and confirmed human-to-human transmission
Initiate emergency surveillance
Number of confirmed cases
Date of onset
First Stage (before Jan. 14, 2020)
Second Stage (Jan. 15-28, 2020)
Third Stage (after Jan. 29, 2020)

C



D

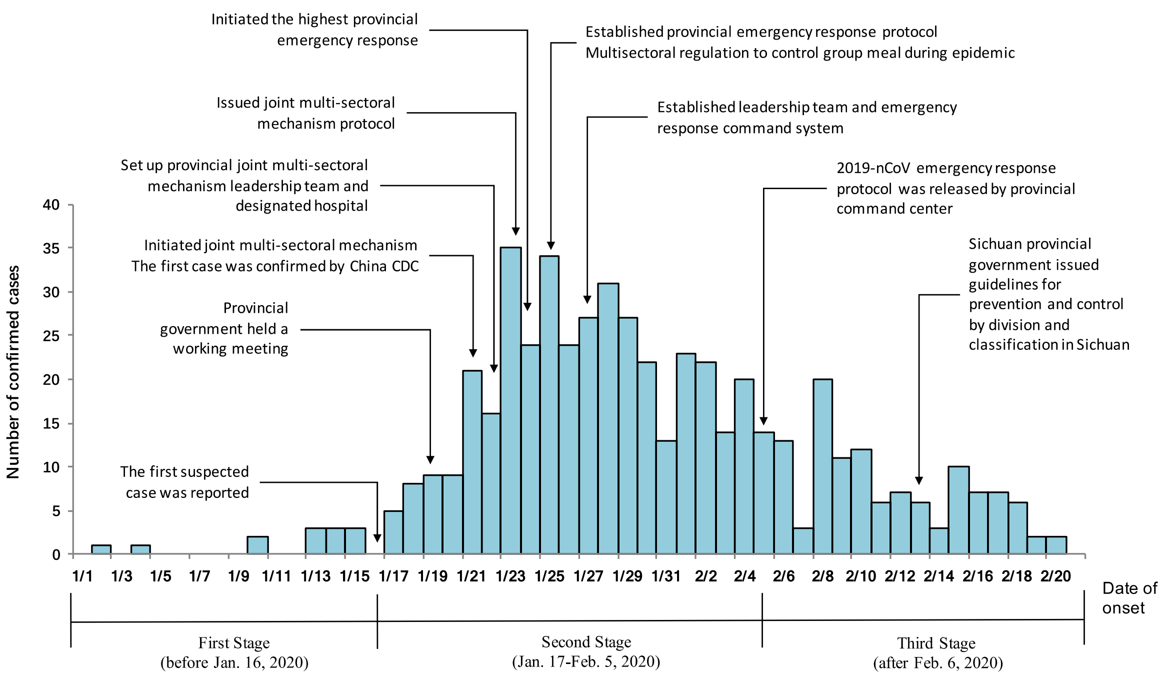


Figure 6. COVID-19 epidemic curves and major intervention measures in China as implemented at a) the national level b) in Guangdong province, c) in Shenzhen municipality and d) in Sichuan province

Risk communications (information release, public and media communications)

International and interregional cooperation and information sharing: From 3 January 2020, information on COVID-19 cases has been reported to WHO daily. Full genome sequences of the new virus were shared with WHO and the international community immediately after the pathogen was identified on 7 January. On 10 January, an expert group involving Hong Kong, Macao and Taiwanese technical experts and a World Health Organization team was invited to visit Wuhan. A set of nucleic acid primers and probes for PCR detection for COVID-19 was released on 21 January.

Daily updates: The National Health Commission announces the epidemic situation every day and holds daily press conferences to respond to emerging issues. The government also frequently invites experts to share scientific knowledge on COVID-19 and to address public concerns.

Psychological care: This is provided to patients and the public. Governments at all levels, NGOs and all sectors of society developed guidelines for emergency psychological crisis intervention and guidelines for public psychological self-support and counselling. A hotline for mental health services has been established for the public.

IT platform: China has capitalized on the use of technology, big data and AI for COVID-19 preparedness, readiness and response. Authoritative and reliable information, medical guidance, access to online services, provision of educational tools and remote work tools have been developed in and used across China. These services have increased accessibility to health services, reduced misinformation and minimized the impact of fake news.

Social mobilization and community engagement

Civil society organizations (community centers and public health centers) have been mobilized to support prevention and response activities. The community has largely accepted the prevention and control measures and is fully participating in the management of self-isolation and enhancement of public compliance. Community volunteers are organized to support self-isolation and help isolated residents at home to solve practical life difficulties. Measures were taken to limit the movement of the population through home-based support. Up to now, outside of Hubei, 30 provinces have registered and managed more than 5 million people coming from Wuhan.

Clinical case management and infection prevention and control

The main **signs and symptoms** of COVID-19 include fever, dry cough, fatigue, sputum production, shortness of breath, myalgia or arthralgia, sore throat, and headache. Nausea or vomiting has been reported in a small percentage of patients (5%). On 14 February, China CDC described the clinical features, outcomes, laboratory and radiologic findings of 44 672 laboratory-confirmed cases. Only 965 (2.2%) were under 20 years of age and there is just one recorded death (0.1%) in this age group. Most patients (77.8%) were aged 30 to 69 years. Patients aged over 80 years had a CFR of 14.8%. The CFR was highest in those with

comorbidities including cardiovascular, diabetes, chronic respiratory disease, hypertension and cancer.

As opposed to Influenza A(H1N1)pdm09, **pregnant women** do not appear to be at higher risk of severe disease. In an investigation of 147 pregnant women (64 confirmed, 82 suspected and 1 asymptomatic), 8% had severe disease and 1% were critical.

Severe cases are defined as tachypnoea (≧30 breaths/ min) or oxygen saturation ≤93% at rest, or PaO2/FIO2 <300 mmHg. **Critical cases** are defined as respiratory failure requiring mechanical ventilation, shock or other organ failure that requires intensive care. About a quarter of severe and critical cases require mechanical ventilation while the remaining 75% require only oxygen supplementation.

China has a principle of **early identification**, early isolation, early diagnosis and early treatment. Early identification of suspect cases is critical to containment efforts and occurs via a process of temperature screening and questioning at entrances to many institutions, communities, travel venues (airports, train stations) and hospitals. Many hospitals have fever clinics that were established and maintained since the SARS outbreak. In China, laboratory tests were originally requested according to the case definitions, which included an epidemiological link to Hubei or other confirmed cases. However, more recently, a more **liberal clinical testing regimen** allows clinicians to test with a low index of suspicion.

Suspect cases are isolated in normal pressure single rooms, wear a surgical mask (for source control). Staff in China wear a cap, eye protection, n95 masks, gown and gloves (single use only). In Wuhan it is necessary for most suspects to be cohorted in a normal pressure isolation ward. Staff wear PPE continuously, changing it only when they leave the ward.

PCR test results are returned the same day. If positive, patients are transported to designated hospitals (including negative pressure ambulances in some cities). All patients, including the mild and asymptomatic, with a positive test are admitted. The designated hospitals are known and are strategically placed with at least one per district/county. Positive cases are cohorted by gender. Negative tested patients are managed based on clinical needs. All patients are evaluated with a respiratory multiplex to look for other diagnoses. This can add to the reassurance that a negative COVID-19 test reflects a lack of infection with COVID-19.

In Wuhan, there are 45 **designated hospitals**, 6 of which are designated for critical patients, and 39 for severe patients and/or any patients >65 years old. There are an additional 10 temporary hospitals reconstructed from gymnasium and exhibition centers, which are for mild patients. Other surge measures undertaken in Wuhan include two new temporary hospitals with 2600 beds, plus many makeshift hospitals to increase bed capacity. Bed capacity within Wuhan has increased to >50,000.

Patients are treated according to the **National Clinical guidelines** (edition 6) released by the China National Health Commission (NHC). There are no specific antiviral or immune modulating agents proven (or recommended) to improve outcomes. All patients are monitored by regular pulse oximetry. The guidelines include supportive care by clinical category (mild, moderate, severe and critical), as well as the role of investigational

treatments such as chloroquine, phosphate, lopinavir/ritonavir, alpha interferon, ribavirin, arbidol. The application of intubation/invasive ventilation and ECMO in critically ill patients can improve survival. The Joint Mission Team was told of ECMO use in four patients at one hospital with one death and three who appeared to be improving. Clearly, though ECMO is very resource consumptive, any health system would need to carefully weigh the benefits. There is widespread use of Traditional Chinese Medicines (TCM), for which the affects must be fully evaluated.

Patients with COVID-19 are not permitted **visitors**. Staff use coveralls, masks, eye cover, and gloves, removing PPE only when they leave the ward.

Patients are discharged after clinical recovery (afebrile >3 days, resolution of symptoms and radiologic improvement) and 2 negative PCR tests taken 24 hours apart. Upon discharge, they are asked to minimise family and social contact and to wear a mask. There are expectations of clinical trial results within a matter of weeks, which will see further opportunities for treatment.

There are guidelines for **elderly care** specifically targeting prevention in individuals and introduction of COVID-19 to nursing homes.

Training programmes by video conference nationally are scaled up to inform staff of best practice and to ensure PPE usage. **Clinical champions** are created to disperse knowledge and provide local expertise.

Maintenance of usual healthcare activities is maintained by hospital zoning (e.g. clean/contaminated sections of the healthcare facility).

Laboratory, diagnostics and virology

The virus found to cause COVID-19 was initially isolated from a clinical sample on 7 January. It is notable that within weeks following the identification of the virus, a series of reliable and sensitive **diagnostic tools** were developed and deployed. On 16 January, the first RT-PCR assays for COVID-19 were distributed to Hubei. Real-time PCR kits were distributed to all the provinces on 19 January and were provided to Hong Kong SAR and Macao SAR on 21 January. Information regarding viral sequences and PCR primers and probes was shared with WHO and the international community by China CDC on 12 January 2020. To facilitate product development and research on the new virus, COVID-19 virus sequences were uploaded to the GISAID Database by China.

By 23 February, there were 10 kits for detection of COVID-19 approved in China by the NMPA, including 6 RT-PCR kits, 1 isothermal amplification kit, 1 virus sequencing product and 2 colloidal gold antibody detection kits. Several other tests are entered in the emergency approval procedure. Currently, there are at least 6 local producers of PCR test kits approved by NMPA. Overall, producers have the capacity to produce and distribute as many as 1,650,000 tests/week.

Specimens from both the upper respiratory tract (URT; nasopharyngeal and oropharyngeal) and lower respiratory tract (LRT; expectorated sputum, endotracheal aspirate, or bronchoalveolar lavage) are collected for COVID-19 testing by PCR.

COVID-19 virus has been detected in respiratory, fecal and blood specimens. According to preliminary data from Guangzhou CDC as of 20 February, virus can initially be detected in upper respiratory samples 1-2 days prior to symptom onset and persist for 7-12 days in moderate cases and up to 2 weeks in severe cases. Viral RNA has been detected in feces in up to 30% of patients from day 5 following onset of symptoms and has been noted for up to 4-5 weeks in moderate cases. However, it is not clear whether this correlates with the presence of infectious virus. While live virus has been cultured from stool in some cases, the role of fecal-oral transmission is not yet well understood. COVID-19 has been isolated from the clinical specimens using human airway epithelial cells, Vero E6 and Huh-7 cell lines.

Serological diagnostics are rapidly being developed but are not yet widely used. Joint Mission members met with local research teams at the China CDC, Guangzhou Regenerative Medicine and Health Guangdong Laboratory. The teams reported on the development of tests for IgM, IgG and IgM+IgG using rapid test platforms utilizing chemiluminiscence. ELISA assays are also under development.

Research & Development

The government of China has initiated a series of major emergency research programs on virus genomics, antivirals, traditional Chinese medicines, clinical trials, vaccines, diagnostics and animal models. Research includes fundamental basic research and human subjects research. For the purpose of this report, human studies are limited to those involving IRB approval and informed consent. Other forms of human subjects investigations are included in the sections on epidemiology in this report. Well-focused, robust research conducted in the setting of an outbreak has the potential of saving many lives by identifying the most effective ways to prevent, diagnose and treat disease.

Since the COVID-19 virus has a genome identity of 96% to a bat SARS-like coronavirus and 86%-92% to a pangolin SARS-like coronavirus, an animal source for COVID-19 is highly likely. This was corroborated by the high number of RT-PCR positive environmental samples taken from the Huanan Seafood Market in Wuhan.

At least 8 **nucleic acid-based methods** for direct detection of COVID-19 and two colloidal gold antibody detection kits have been approved in China by the NMPA. Several other tests are close to approval. It will be important to compare the sensitivities and specificities of these and future serologic tests. Development of rapid and accurate **point-of-care tests** which perform well in field settings are especially useful if the test can be incorporated into presently commercially available multiplex respiratory virus panels. This would markedly improve early detection and isolation of infected patients and, by extension, identification of contacts. **Rapid IgM and IgG antibody testing** are also important ways to facilitate early diagnosis. Standard serologic testing can be used for retrospective diagnoses in the context of serosurveys that help better understand the full spectrum of COVID-19 infection.

A variety of **repurposed drugs and investigational drugs** have been identified. Screening NMPA approved drug libraries and other chemical libraries have identified novel agents. Hundreds of clinical trials involving remdesivir, chloroquine, favipiravir, chloroquine, convalescent plasma, TCM and other interventions are planned or underway. Rapid completion of the most important of these studies is critical to identifying truly effective therapies. However, evaluation of investigational agents requires adequately powered, randomized, controlled trials with realistic eligibility criteria and appropriate stratification of patients. It is important for there to be a degree of coordination between those conducting studies within and beyond China.

The development of a safe and effective **vaccine** for this highly communicable respiratory virus is an important epidemic control measure. Recombinant protein, mRNA, DNA, inactivated whole virus and recombinant adenovirus vaccines are being developed and some are now entering animal studies. Vaccine safety is of prime concern in the area of coronavirus infection in view of the past experience of disease enhancement by inactivated whole virus measles vaccine and similar reports in animal experiments with SARS coronavirus vaccines. It will be important that these vaccine candidates rapidly move into appropriate clinical trials.

The ideal **animal model** for studying routes of virus transmission, pathogenesis, antiviral therapy, vaccine and immune responses has yet to be found. The ACE2 transgenic mouse model and Macaca Rhesus model are already used in research laboratories. Systematically addressing which models can accurately mimic human infection is required.

There is a global rush for masks, hand hygiene products and other personal protective equipment. The relative importance of **non-pharmaceutical control measures** including masks, hand hygiene, and social distancing require further research to quantify their impact.

There are distinct patterns of intra-familial transmission of COVID-19. It is unclear whether or not there are host factors, including genetic factors, that influence susceptibility or disease course. COVID-19 has a varied clinical course and a precise description of that course is not available. In addition, the long-term consequences of COVID-19 are unknown. An observational cohort study of patients with COVID-19 enrolled from the time of diagnosis (with appropriate controls) could provide in-depth information about clinical, virologic and immunologic characteristics of COVID-19. Table 1 summarizes priority research areas with immediate to longer term goals.

Table 1 Priority research areas with immediate, intermediate and longer-term goals

Immediate Goals	Intermediate Goals	Long-term goals
Diagnostics: RNA assays, antibody & antigen assays, point of care detection	Diagnostics: Multiplex diagnostic platforms	Diagnostics: Prognostic markers
Therapeutics: Remdesivir, favipiravir, chloroquine, plasma, TCM	Therapeutics: intravenous immunoglobulin (IVIg)	Therapeutics: Innovative approaches (CRISPR-CAS; RNAi; Cell-based; positive hits from library screening)
Vaccines: Development of animal models	Vaccines: mRNA candidates and candidate viral vectors	Vaccines: inactivated candidates and subunit candidates

D. Knowledge Gaps

Knowledge gaps and key questions to be answered to guide control strategies include:

Source of infection

- Animal origin and natural reservoir of the virus
- Human-animal interface of the original event
- Early cases whose exposure could not be identified

The pathogenesis and virulence evolution of the virus

Transmission dynamics

- Modes of Transmission:
    - Role of aerosol transmission in non-health care settings
    - Role of fecal-oral transmission
- Viral shedding in various periods of the clinical course in different biological samples (i.e. upper and lower respiratory tract, saliva, faeces, urine)
    - Before symptom onset and among asymptomatic cases
    - During the symptomatic period
    - After the symptomatic period / during clinical recovery

Risk factors for infection

- Behavioral and socio-economic risk factors for infection in
    - Households / institutions
    - the Community
- Risk factors for asymptomatic infection
- Risk factors for nosocomial infection
    - among health care workers
    - among patients

Surveillance and monitoring

- Monitoring community transmission through existing
    - ILI surveillance
    - SARI surveillance
- The outbreak trend and intervention dynamics
    - Basic reproduction numbers in various stages of the epidemic
    - The epidemic's relation to seasonality

Laboratory and diagnostics

- Sensitivity and specificity of different nucleic acid (PCR, NAATs and rapid tests), antibody and antigen tests
- Post-infection antibody titers and the duration of protection
- Sero-prevalence among
    - Health care workers
    - General population
    - Children

Clinical management of severe and critically ill patients

- Value of ECMO in the management of critically ill patients
- Best practice using mechanical ventilation in the management of critically ill patients
- Re-evaluation of the role of steroids in the management of severe and critically ill patients
- Identification of factors associated with successful clinical management and outcome
- Determination of the effectiveness of Traditional Chinese Medicines (TCM)
- Determination the effectiveness of additional investigational treatment options (e.g. intravenous immunoglobulin/IVIg, convalescent plasma)

Prevention and control measures

- Key epidemic indicators that inform evidence-based control strategy decision making and adjustments
- Effectiveness of infection prevention and control (IPC) measures in various health care settings
- Effectiveness of entry and exit screening
- Effectiveness of the public health control measures and their socio-economic impact
    - Restriction of movement
    - Social distancing
    - School and workplace closures
    - Wearing mask in general public
    - Mandatory quarantine
    - Voluntary quarantine with active surveillance

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E. Operational & Technical Recommendations

Operational/programmatic recommendations

- Reassess risk and capacities based on different stages of the outbreak; approve different measures during the different phases of the response; assess different stages of the response; reach a balance between response and social development
- Initiate a timely scientific evidence based, efficient and flexible joint multi-sectoral mechanism, which is driven by strong government leadership

Technical recommendations

Epidemiology and transmission

- Continue enhanced surveillance across the country through existing respiratory disease systems, including ILI, SARI or pneumonia surveillance systems
- Prioritize early investigations, including household transmission studies, age-stratified sero-epidemiologic surveys including children, case-control studies, cluster investigations, and serologic studies in health care workers

Severity

- Continue to share information on patient management, disease progression and factors leading to severe disease and favorable outcomes
- Review and analyze the possible factors associated with the disease severity, which may include:
  - natural history studies to better understand disease progression in mild, severe and fatal patients
  - medical chart reviews about disease severity among vulnerable groups, (e.g. those with underlying conditions, older age groups, pregnant women and children) to develop appropriate standards of care
  - evaluation of factors leading to favorable outcomes (e.g. early identification and care)

Clinical care and infection prevention and control

- Suspect patients who have not yet been tested should be isolated in single normal pressure rooms; cohorting of positive cases is acceptable
- Physicians and all health care workers need to maintain a high level of clinical alert for COVID-19
- For affected countries, standardize training for clinical care and IPC and scale with the development of local (e.g. district level) experts
- Ensure concurrent testing for other viral pathogens to support a negative COVID-19 test
- Ensure maintenance of usual and essential services during the outbreak

- Ensure processes are in place for infection prevention among the most vulnerable, including the elderly
- Ensure readiness to provide clinical care and to meet IPC needs, including:
    a. anticipated respiratory support requirements (e.g. pulse oximeters, oxygen, and invasive support where appropriate)
    b. national guidelines for clinical care and IPC, revised for COVID-19
    c. nationally standardised trainings for disease understanding and PPE use for HCWs
    d. community engagement
    e. PPE and Medication stockpiles
    f. early identification protocols; triage, temperature screening, holding bays (triage, including pulse oximetry)
    g. treatment protocols including designated facilities, patient transportation
    h. enhanced uptake of influenza and pneumococcal vaccine according to national guidelines
    i. laboratory testing
    j. rapid response teams

Laboratory and virology

- Continue to perform whole genome analysis of COVID-19 viruses isolated from different times and places, to evaluate virus evolution
- Conduct pathogenesis studies using biopsy/post-mortem specimens of COVID-19 patients or infected animal models
- Evaluate available nucleic acid PCR diagnostics
- Rapidly develop and evaluate rapid/point-of-care diagnostics and serologic assays
- Conduct further study to interpret the result of positive COVID-19 RNA detection in feces in patients recovering from COVID-19
- Enhance international cooperation, especially in terms of biosafety and information sharing for increased understanding of the COVID-19 virus and traceability of the virus
- Consider monitoring proinflammatory cytokines via multiplex assays to predict the development of "cytokine storm"

Research and development

- Additional effort should be made to find the animal source, including the natural reservoir and any intermediate amplification host, to prevent any new epidemic foci or resurgence of similar epidemics

- Efforts should be made to consistently evaluate existing and future diagnostic tests for detection of COVID-19 using a harmonized set of standards for laboratory tests and a biorepository that can be used for evaluating these tests
- Consider the establishment of a centralized research program in China to oversee that portfolio and ensure the most promising research (vaccines, treatments, pathogenesis) are adequately supported and studied first; program staff dedicated to the clinical research would work at the clinical research site(s) to decrease the research workload of the clinicians at the site
- Consider including one or more sites within China in the ongoing and future multi-center, international trials; Chinese investigators should be actively engaged in international trials
- Continue to develop additional animal models, making every effort to ensure these mimic human infection and virus transmission as closely as possible
- Conduct studies to determine which of the commonly used forms of PPE are most effective in controlling the spread of COVID-19